TECHNOLOGY TRANSFER-WHO GUIDELINES

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Syllabus

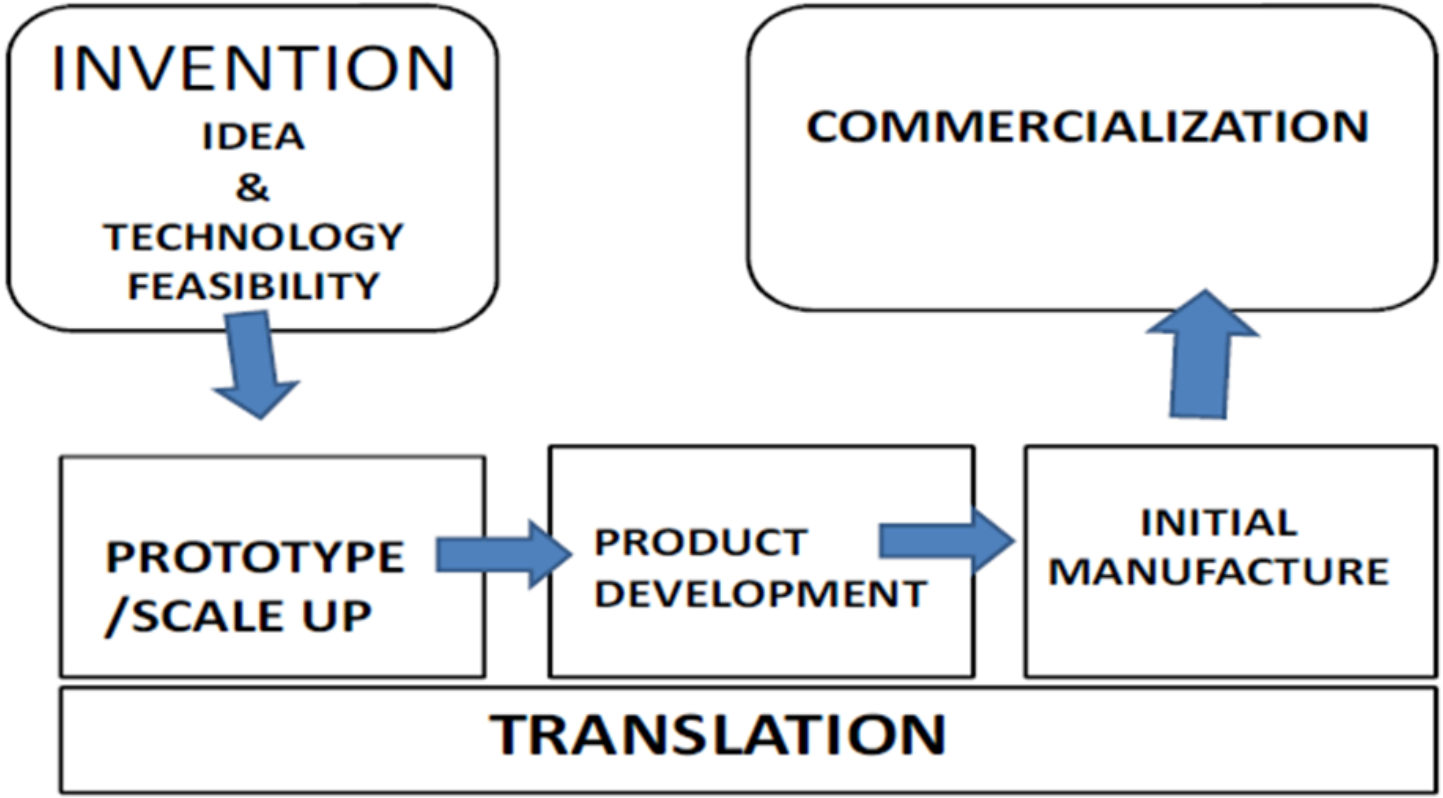
Technology development and transfer:

WHO Guidelines for Technology Transfer (TT): Terminology, Technology transfer protocol, Quality risk management, Transfer from R & D to production (Process, packaging and cleaning), Granularity of TT Process (API, excipients, finished products, packaging materials), Documentation, Premises and equipment, qualification and validation, quality control, analytical method transfer, Approved regulatory bodies and agencies, Commercialization - practical aspects and problems (case studies), TT agencies in India - APCTD, NRDC, TIFAC, BCIL, TBSE / SIDBI; TT-related documentation - confidentiality agreement, licensing, MoUs, legal issues

Introduction

- Transfer of technology is defined as a “logical procedure that controls the transfer of any process together with its documentation and professional expertise between developments or between manufacture sites”.
- Technology transfer is both integral and critical to the drug discovery and development process for new medical products.
- Technology transfer facilitates efficient, high-quality, and cost-effective development of dosage forms by making innovative technology available to commercial partners.

- In the pharmaceutical industry, “Technology transfer” refers to the processes of successful progress from drug discovery to product development, clinical trials and ultimately full-scale commercialization.
- Technology transfer is important for such researchers to materialize on a larger scale for commercialization, especially in the case of developing products.
- Technology transfer includes not only patentable aspects of production but also includes business processes such as knowledge and skills.


INVENTION
IDEA
&
TECHNOLOGY
FEASIBILITY
COMMERCIALIZATION
PROTOTYPE
/SCALE UP
PRODUCT
DEVELOPMENT
INITIAL
MANUFACTURE
TRANSLATION

Purpose

- The purpose of technology transfer is to strengthen the economy by accelerating the application of laboratory technology and resources to private and public needs and opportunities.
- Successful technology transfer efforts result in product improvement, service efficiencies, improved manufacturing processes, joint development to address government and private sector needs, and the development of major new products for the international marketplace.

Terminology

- **Acceptance criteria:** Measurable terms under which test results will be considered acceptable.
- **Bracketing:** An experimental design to test only the extremes of, for example, dosage strength. The design assumes that the extremes will be representative of all the samples between the extremes.
- **Change control (C/C):** A formal system by which qualified representatives of appropriate disciplines review proposed or actual changes that might affect a validated status. The intent is to determine the need for action that would ensure that the system is maintained in a validated state.

- **Commissioning:** The setting up, adjustment and testing of equipment or a system to ensure that it meets all the requirements, as specified in the user requirement specification, and capacities as specified by the designer or developer. Commissioning is carried out before qualification and validation.
- **Corrective action (C/A):** Any action to be taken when the results of monitoring at a critical control point indicate a loss of control.
- **Critical:** Having the potential to impact product quality or performance in a significant way.
- **Critical control point (CCP):** A step at which control can be applied and is essential to prevent or eliminate a pharmaceutical quality hazard or reduce it to an acceptable level.

- **Design qualification (DQ):** Documented evidence that the premises, supporting systems, utilities, equipment and processes have been designed in accordance with the requirements of good manufacturing practices (GMP).
- **Design space:** The multidimensional combination and interaction of input variables (e.g. material attributes) and process parameters that have been demonstrated to provide assurance of quality.
- **Drug master file (DMF):** Detailed information concerning a specific facility, process or product submitted to the drug regulatory authority, intended for incorporation into the application for marketing authorization.

- **Gap analysis:** Identification of critical elements of a process which are available at the SU but are missing from the RU.
- **Good Manufacturing Practices (GMP):** That part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.
- **Inter-company transfer:** A transfer of technology between sites of different companies.
- **Intra-company transfer:** A transfer of technology between sites of the same group of companies.
- **In-process control (IPC)** Checks performed during production to monitor and, if necessary, to adjust the process to ensure that the product conforms to its specifications. The control of the environment or equipment may also be regarded as a part of in-process control.

- **Installation qualification (IQ):** The performance of tests to ensure that the installations (such as machines, measuring devices, utilities and manufacturing areas) used in a manufacturing process are appropriately selected and correctly installed and operate in accordance with established specifications.
- **Operational qualification (OQ):** Documented verification that the system or subsystem performs as intended overall anticipated operating ranges.
- **Performance qualification (PQ):** Documented verification that the equipment or system operates consistently and gives reproducibility within defined specifications and parameters for prolonged periods.

- **Process validation:** Documented evidence which provides a high degree of assurance that a specific process will consistently result in a product that meets its predetermined specifications and quality characteristics.
- **Quality assurance (QA):** Quality assurance is a wide-ranging concept covering all matters that individually or collectively influence the quality of a product. The totality of the arrangements made to ensure that pharmaceutical products are of the quality required for their intended use.
- **Quality control (QC):** Quality control covers all measures taken, including the setting of specifications, sampling, testing and analytical clearance, to ensure that starting materials, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics.

- **Qualification:** Action of proving and documenting that any premises, systems and equipment are properly installed, and/or work correctly and lead to the expected results. Qualification is often a part (the initial stage) of validation, but the individual qualification steps alone do not constitute process validation.
- **Quality risk management (QRM):** Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the pharmaceutical product across the product life-cycle.
- **Receiving unit (RU):** The involved disciplines at an organization where a designated product, process or method is expected to be transferred.

- **Sending unit (SU):** The involved disciplines at an organization where a designated product, process or method is expected to be transferred from.
- **Spiking:** The addition of a known amount of a compound to a standard, sample or placebo, typically to confirm the performance of an analytical procedure.
- **Standard operating procedure (SOP):** An authorized written procedure giving instructions for performing operations not necessarily specific to a given product or material (e.g. equipment operation, maintenance and cleaning; validation; cleaning of premises and environmental control; sampling and inspection).

- **Transfer of technology (TOT):** A logical procedure that controls the transfer of an established process together with its documentation and professional expertise to a site capable of reproducing the process and its support functions to a predetermined level of performance.
- **Validation:** Action of proving and documenting that any process, procedure or method actually and consistently leads to the expected results.
- **Validation master plan (VMP):** A high-level document that establishes an umbrella validation plan for the entire project and summarizes the manufacturer's overall philosophy and approach, to be used for establishing performance adequacy. It provides information on the manufacturer's validation work programme and defines details of and timescales for the validation work to be performed, including a statement of the responsibilities of those implementing the plan.

- **Validation protocol (or plan) (VP):** A document describing the activities to be performed in a validation, including the acceptance criteria for the approval of a manufacturing process or a part thereof for routine use.
- **Validation report (VR):** A document in which the records, results and evaluation of a completed validation programme are assembled and summarized. It may also contain proposals for the improvement of processes and/or equipment.

Technology Transfer Protocol

- The protocol is concerned with transferring technology from (i) R&D to the manufacturing site, and from one manufacturing site to another manufacturing site.
- This procedure is applicable for the technology transfer of process, method, and knowledge from the development stage to the manufacturing site or from one manufacturing site to another.

Major areas of Technology Transfer Protocol (Both sending site & Receiving site):

i. A comparison of material, method, and equipment with details of the action plan, if any difference is observed.

ii. The transfer stages with documented evidence that each stage/critical stage has been satisfactorily accomplished before the next commences.
iii. Identification of critical control points.
iv. Experimental design and acceptance criteria for the analytical method.
v. Project plan for trial batches (optimization batches), qualification batches and process validation batches.
vi. Training and skill development
vii. Protocol approval.

- The transfer protocol should list the intended sequential stages of the transfer.
- The protocol should include:

❖ Objective
❖ Scope
❖ Key personnel and their responsibilities
❖ A parallel comparison of materials, methods and equipment
❖ The transfer stages with documented evidence that each critical stage has been satisfactorily accomplished before the next commences
❖ Identification of critical control points
❖ Experimental design and acceptance criteria for analytical methods
❖ Information on trial production batches, qualification batches and process validation

- ❖ Change control for any process deviations encountered
- ❖ Assessment of end-product
- ❖ Arrangements for keeping retention samples of active ingredients, intermediates and finished products, and information on reference substances where applicable; and
- ❖ Conclusion, including signed-off approval by the project manager.

- SU should provide the necessary validation documentation for the process and its support functions.
- SU should also provide criteria and information on hazards and critical steps associated with the product, process or method to be transferred, to serve as the basis for a quality risk management (QRM) exercise at RU.

- SU or a third party should assess the suitability and degree of preparedness of the RU before the transfer, of premises, equipment and support services (e.g, purchasing and inventory control mechanisms, quality control procedures, documentation, computer validation, site validation, equipment qualification, water for pharmaceutical production and waste management.
- A final technology transfer summary report with a conclusion should be prepared and finally agreed upon & approved by the sending site and receiving site stakeholders.
- Any changes during technology transfer should be handled through a change control procedure followed by risk assessment.